Original Articles

Are racial differences in hospital mortality after coronary artery bypass graft surgery real? A risk adjusted meta-analysis.

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Central message: Despite progress is being made in lowering in-hospital mortality rates among the major racial/ethnic groups, ethnical disparities in hospital mortality after coronary bypass surgery remain.

Prospective statement: The effect of race on mortality after coronary bypass surgery remains uncertain and current guidelines and risk stratification systems make no differentiation by race. We showed that despite progress is being made in lowering in-hospital mortality rates among the major racial/ethnic groups, ethnical disparities in hospital mortality after CABG remain.

ABBREVIATIONS

CABG: coronary artery bypass grafting

CI: confidence interval

OR: odds ration

Abstract

Background: Despite several reports**,** there are still conflicting data on the influence of ethnicity on mortality rates associated with coronary artery bypass grafting (CABG). We aimed to get further insights into the effect of race on mortality following CABG by performing a risk adjusted meta-analysis.

Methods: Relevant studies were searched on PubMed, Embase, BioMed Central, and the Cochrane Central register. Pairwise meta-analysis was used to estimate the relative risk of hospital death of black, Hispanic and Asiatic patients using White patients as reference. Risk adjusted meta-analytic estimates were obtained using generic inverse variance methods with random effect model.

Results: A total of twenty-eight studies were selected for analysis. A total of twenty-one studies reported on hospital mortality in Black (n=222,892) versus White (n=3,884,043) patients, seven studies reported on Hispanic (n=91,256) versus White (n= 1,458,524) and nine studies reported on Asiatic (n=27,820) versus White (n=1,081,642). When compared to White patients, adjusted risk of hospital death was significantly higher for Black patients (adjusted OR 1.25; 95%CI 1.13-1.39; $P<0.001$), and not statistically different for Asiatic (OR 1.33; 95%CI 0.99, 1.77; $P=0.05$) and Hispanic patients (adjusted OR 1.08; 95%CI 0.94- 1.23; $P=0.26$). Meta-regression showed a significant trend towards lower mortality rates in most recent series in both Blacks ($P=0.02$) and Whites ($P=0.0007$) and Asiatic ($P=0.01$) but not for Hispanic ($P=0.41$). However, as mortality rates were lower across the different races, the relative disadvantage between the study groups persisted, which may explain the lack of interaction between study period and race effect on mortality for Black (adjusted $P=0.09$), Asiatic (adjusted $P=0.63$) and Hispanic (adjusted $P=0.97$).

Conclusions: The present meta-analysis showed that despite progress is being made in lowering in-hospital mortality rates among the major racial/ethnic groups, ethnical disparities in hospital mortality after CABG remain.

Introduction

Although multiple studies have found that non-White patients, in particular Black and Hispanic, have lower rates of cardiovascular procedures, including cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting (CABG) [1], there are still limited and conflicting data on the influence of ethnicity on mortality and complication rates associated with CABG [2-6]. One potential concern is that if racial minorities are less likely to be referred for cardiac catheterization and coronary revascularization, then only those with particularly advanced disease or compelling indications may undergo these procedures, leading to worse outcomes [2-4]. Previous studies evaluating the impact of ethnicity on mortality following CABG surgery have had mixed conclusions. Several studies have reported higher mortality for Black patients following the operation [5,6]. Other studies, have suggested similar risk adjusted survival for Black patients following CABG surgery [2-4]. Therefore, the effect of race on mortality after CABG remains uncertain [2] and current CABG guidelines [7] and risk stratification systems [8,9] make no differentiation by race. We aimed to get further insights into the effect of race on mortality following CABG by performing a risk adjusted meta-analysis of comparative studies.

Methods

Literature Search Strategy

The search strategy adopted is in accordance with the Meta-analysis of Observational Studies in Epidemiology guidelines [10]. We searched PubMed, the Cochrane Central Register of Controlled Trials, and EMBASE from their inception to March 2017, without language restrictions. Search algorithm used was "race" OR "ethnicity" AND ("coronary artery bypass"

OR CABG OR "bypass surgery" OR "coronary bypass"). In addition, reference lists of the identified reports and relevant reviews were manually screened by 2 reviewers (UB, MK) to identify relevant studies. Studies reporting hospital outcomes after CABG across different ethnical groups including White, Black, Hispanic and Asiatic were selected. When centres have published duplicate trials with accumulating numbers of patients, only the largest reports were included for qualitative appraisal. Non-English articles were not excluded. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Disagreements were resolved by consensus. The quality of included studies was assessed with the Newcastle-Ottawa scale for observational studies [11]. The total score was 9 stars, and the quality was graded as low level (<6 stars) or high level (≥6 stars). Baseline characteristics and hospital outcomes in different ethnical groups were independently abstracted by 2 investigators (UB, MK). The primary outcome of the present meta-analysis was hospital mortality. Hospital mortality crude incidence rate for different ethnical groups were obtained from individual studies. As different ethnical groups can present different patient level and hospital level factors distribution, we also extracted fully adjusted estimates obtained by multivariate models from individual studies. Other operative outcomes investigated were: stroke, wound infection, renal failure/dialysis, re-exploration for bleeding, respiratory failure/tracheostomy.

Statistical analysis

Pairwise meta-analysis methods were used to estimate operative mortality relative risk for different ethnical groups (Black, Hispanic and Asiatic) using White group as reference. A subgroup analysis was done to compare South Asian to White. Individual study and pooled operative mortality was reported as odds ratio (OR) with a 95% confidence interval (CI). Unadjusted pooled estimates were obtained using DerSimonian and Laird model [12]. Individual studies risk-adjusted estimates were pooled as log OR and standard error (SE) using generic inverse variance method [13]. Random effect was used in all meta-analyses to obtain more conservative estimates [14] We used the I^2 statistic, which estimates the percentage of total variation across studies that is due to heterogeneity rather than chance. Suggested thresholds for heterogeneity were used, with I2 values of 25–49%, 50–74% and ≥75%, indicative of low, moderate and high heterogeneity [15, 16]. For each study, median year of enrolment was obtained and changes in estimates across different eras were tested using meta-regression model (Mixed-Effects Model). Meta-analytic estimates were computed using Review Manager (RevMan, Computer program. Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) and meta R package (R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Results

Study selection

A total of 1362 references were identified through electronic database searches and references lists. After exclusion of duplicate or irrelevant references, 45 potentially relevant articles were retrieved. After detailed evaluation of these articles, 28 studies were selected for analysis [2-6,16-38] (Figure). Study overview, patients' characteristics and severity of coronary artery disease are reported in Table 1, Table 2 and Supplementary Table 1, respectively. A total of twenty-one studies reported on hospital mortality in Black (n=222,892) versus White (n=3,884,043) patients, seven studies reported on Hispanic (n=91,256) versus White (n= 1,458,524) and nine studies reported on Asiatic (n=27,820) versus White (n=1,081,642). Of the nine studies that reported on Asiatic patients, five studies reported on South Asians, one study reported on South Asians and Chinese, and three studies did not distinguish between the different Asiatic ethnicities. Fully adjusted estimates including patients level and hospital level covariates were reported by 12 studies for Black vs White comparison, 4 studies for Hispanic vs White comparison and 4 studies for Asiatic vs White comparison. The methods and variables used in adjustment are listed in Supplementary Table 2. Quality assessment of individual studies is reported in Table 3.

Meta-analysis

Meta-analysis of unadjusted rates (Figure 2) showed that when compared to White patients, Black (unadjusted OR 1.24; 95%CI 1.20-1.28; P<0.001) and Asiatic patients (unadjusted OR 1.33; 95%CI 1.05-1.69; P=0.02) were associated with a significantly increased risk for hospital death while Hispanic presented a comparable risk (unadjusted OR 0.98; 95%CI 0.87-1.09; P=0.66). This trend was confirmed when reported adjusted estimates for hospital mortality were pooled (Figure 3). When compared to White patients, adjusted risk of hospital death was significantly higher for Black patients (adjusted OR 1.25; 95%CI 1.13-1.39; P<0.001), and not statistically different for Asiatic (OR 1.33; 95%CI 0.99, 1.77; P=0.05) and Hispanic patients (adjusted OR 1.08; 95%CI 0.94- 1.23; P=0.26).

A subgroup analysis showed that South Asians had higher risk of crude hospital mortality compared to Whites (unadjusted OR 1.72; 95%CI 1.12-2.66; P=0.01). However, there was no difference in the risk of hospital mortality between South Asians and Whites after adjusting for possible confounding factors (adjusted OR: 1.73; 95%CI 0.71-4.18; P=0.23) (Supplementary Figure 1).

Meta-regression (Figure 4) showed a significant trend towards lower mortality rates in most recent series in both Blacks (P=0.02) and Whites (P=0.0007) and Asiatic (P=0.01) but not for Hispanic (P=0.41). However, as mortality rates were lower across the different races, the relative disadvantage between the study groups persisted, which may explain the lack of interaction between study period and race effect on mortality for Black (unadjusted P=0.29, adjusted P=0.09), Asiatic (unadjusted P=0.15, adjusted P=0.63) and Hispanic (unadjusted and adjusted P=0.97).

Postoperative complications

For the comparison between Blacks and Whites, several studies reported also on unadjusted rate of postoperative complication (Supplementary Figure 2). Pooled estimates showed that rate for stroke (unadjusted OR 1.78; 95%CI 1.49-2.13; P<0.001), bleeding (unadjusted OR 1.24; 95%CI 1.09-1.41), tracheostomy/reintubation (unadjusted OR 1.37; 95%CI 1.15, 1.61; P=0.0003) and renal failure (adjusted OR 1.54; 95%CI 1.38-1.73; P<0.001) but not wound infection (OR1.16; 95%CI 0.98- 1.36; P=0.09) were higher among Black patients.

Discussion

In the present study, we investigated the effect of race by performing a meta-analysis and meta-regression of comparative studies available. We showed that Black race was associated with increased mortality rates when compared to White race also after adjusting for patient-level and hospital-level factors. We also showed that despite mortality rates declined over the years for Black patients, a specular reduction in mortality was observed for White patients. Therefore the gap between Black and White patients remained stable. Black race was also shown to be associated with significant increased risk of postoperative complications including bleeding, stroke, renal failure/dialysis and respiratory failure/tracheostomy. Although not statistically significant, there was a strong trend towards an increased risk of mortality in Asiatic when compared to White subjects (P =0.05). On the other hand, Hispanics were consistently found to have mortality rates comparable to those observed in Whites without significant changes across different eras.

Despite several studies have suggested ethnical disparities in operative outcomes following CABG [5,6] final conclusions are still lacking and current CABG guidelines and risk stratification systems including the Society of Thoracic Surgeons (STS scoring system) (http://riskcalc.sts.org/stswebriskcalc/) [8] and the European System for Cardiac Operative Risk Evaluation (Euroscore) (http://www.euroscore.org/) [9] make no differentiation by race in terms of operative mortality. The present study consistently demonstrated that Black patients remain associated with a higher operative mortality although this disparity was found to be relevant only among males.

There are a number of possible explanations for these persistent differences in outcomes between the different racial groups. First, it is well documented that disparities in access to health care system persist by race and Black patients are likely to be referred to surgery with poorer health conditions [39-40]. While the present NIS analysis and meta-analysis controlled for many more patient, organizational and socioeconomic aspects of CABG patients' condition, there still may be other unmeasured social phenomena of the patient's background, health condition or hospital stay that may help explain racial/ethnic differences. In addition, many aspects of the physician-patient relationship that involve patients' education, trust and the physician's sensitivity to a patient's culture might also play a critical role [40]. Finally, others have identified genetic differences in race/ethnicity that could account for differences in outcomes. For patients with heart disease, some studies have suggested subtle differences among race/ethnicities in the biology of hypertension. Potential differences in the biology of hypertension may result in more frequent and more severe hypertension and ventricular hypertrophy in Black patients [41].

The present meta-analysis presents several limitations. The vast majority of the included studies didn’t mention the definitions used for race identification, a factor that may have influenced the results. Although we performed a risk-adjusted analysis, we cannot exclude the presence of residual confounding factors accounting for differences in outcomes between ethnical groups, which may have not been considered by individual studies. In particular, data on predicted risk of mortality (i.e. SYNTAX score) were not provided in most of the studies. Moreover, detailed information on patients’ socioeconomic status and surgeon and hospital volume were limited. The study focused primarily on operative mortality and did not compare the differences in long-term outcomes between the different race groups. Most of the series included in the present analysis were from US databases and this might partially limit the generalizability of the present findings. In addition, despite we attempt to avoid cohort overlapping among different studies, we cannot exclude that different US nationwide databases might have reported on similar study populations. Finally, we acknowledge the difficulties and uncertainties that may sometimes be associated with defining individual patients' ethnicities, particularly for those residing in North America where the population diversity may lead to racial mixing.

In conclusion, the present meta-analysis confirmed that despite progress is being made in lowering in-hospital mortality rates among the major racial/ethnic groups including Black patients, significant disparities in outcomes still remains and these warrant further investigation.

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Figure Legend

Central picture: Meta-analytic risk-adjusted estimates of race effect on operative mortality (White as reference)

Figure 1. Study selection process for meta-analysis

Figure 2. Meta-analytic unadjusted estimates of race effect on operative mortality (White as reference)

Figure 3. Meta-analytic risk-adjusted estimates of race effect on operative mortality (White as reference)

Figure 4. Meta-regression of crude mortality rate in separate ethnical groups and race effect on mortality across different study periods (median year of enrolment).

Supplementary Figure 1. Meta-analytic unadjusted and adjusted risk of operative mortality in South Asians compared to Whites.

Supplementary Figure 2. Meta-analytic estimates of unadjusted effect of Black vs White race on postoperative complications.

Table 1. Overview of studies included in the meta-analysis

N of study	First author and year of publication	Country	Single vs multi-institution	Years of enrolment	Information on source of data	White Patients (N)	Black patients (N)	Asiatic patients (N)	Hispanic Patients (N)	Race identification
1	Anderson 2016	USA	multi-institution	2011-2012	California CABG Reporting Program	14389	975	3196	4614	*
2	Andrews 2015	USA	multi-institution	2009	Healthcare Research and Quality (NIS)	194440	15534			*
3	Becker 2006	USA	multi-institution	1993-2002	Healthcare Research and Quality (NIS)	1040641	63991	20353	67554	*
4	Bridges 2000	USA	multi-institution	1994-1997	Society of Thoracic Surgeons (STS)	555939	25850			Self-identified
5	Brister 2007	Canada	Single institution	1994-2003	-	917		917		Self-identified & patients' name
6	Chowdhury 2016	USA	Single institution	2006-2010	-	3107	389			Self-identified
7	Cooper 2009	USA	multi-institution	1997-2007	Society of Thoracic Surgeons (STS)	10841	2033			*
8	Efird 2015	USA	Single institution	1992-2011	-	11395	2379			Self-identified
9	Gasevic 2013	Canada	multi-institution	1999-2003	British Columbia Cardiac Registry	1507		180		Patients' name
10	Goldsmith 1999	UK	Single institution	1994-1997	-	190		194		*
11	Gray 1996	USA	Single institution	1984-1992	-	3113	115			*
12	Hadjinikolaou 2010	UK	Single institution	2002-2007	-	2623		274		Self-identified
13	Kaila 2014	Canada	multi-institution	1999-2012	APPROACH database	737		252		Patients' name
14	Keeling 2016	USA	Single institution	2002-2014	-	13569	2810			*
15	Kim 2008	USA	multi-institution	2002-2005	University HealthSystem Consortium	63487	8462			*
16	Konety 2005	USA	multi-institution	1997-2000	Medicare Provider and Analysis Review	566785	24354			*
17	Lucas 2006	USA/Canada	multi-institution	1994-1999	Medicare Provider and Analysis Review	829037	33367			*
18	Maynard 2001	USA	multi-institution	1994-1999	Veteran Affair	27439	2380			*
19	Mehta 2016	USA	multi-institution	2010-2011	Society of Thoracic Surgeons (STS)	136362	14375			*
20	O'Neal 2014	USA	Single institution	2002-2011	-	3460	970			Self-identified
21	Pollock 2015	USA	Single institution	2004-2011	-	6365	612		593	*

22	Rangrass 2014	USA	multi-institution	2007-2008	Medicare Analysis Provider and Review	159043	9390		3016	*
23	Rumsfeld 2002	USA	multi-institution	1995-2001	Veteran Affair	29333	2570		1525	*
24	Smith 2006	USA	multi-institution	1993-2005	multi-institutional database	1932	644			*
25	Trivedi 2006	USA	multi-institution	1998-2001	Healthcare Research and Quality (NIS)	193684	11393		11393	*
26	Yeo 2007	USA	multi-institution	2003	California CABG Outcomes Reporting Program	15069	785	1772	2561	*
27	Zacharias 2005	USA	Single institution	1991-2003	-	6073	304			*
28	Zindrou 2001	UK	Single institution	1993-1997	-	1458		436		Self-identified
* As reported in single / multiple institutional or national databases										

Table 2. Patients' characteristics in studies included in the meta-analysis

	Mean Age (years)				% Female				% Diabetes Mellitus			
Study	**White**	**Black**	**Asiatic**	**Hispanic**	**White**	**Black**	**Asiatic**	**Hispanic**	**White**	**Black**	**Asiatic**	**Hispanic**
Anderson 2016												
Andrews 2015					27.10%	42.60%						
Becker 2006					28.40%	44%	27.70%	31.40%				
Bridges 2000	65	62			27.93%	44.45%			27.82%	43.78%		
Brister 2007	62		61		23.50%		23.60%		37.30%		39.40%	
Chowdhury 2016	58	56			10%	21%						
Cooper 2009	63	60			27%	42%			33.60%	47.00%		
Efird 2015	65	62			27.30%	42%			32.00%	48.00%		
Gasevic 2013					21%		18%		21.30%		31.00%	
Goldsmith 1999	58		58						11.60%		38.70%	
Gray 1996	67	65			21%	35%			23.00%	36.00%		
Hadjinikolaou 2010	66		63		19.70%		23%					
Kaila 2014					20.30%		21.40%		47.80%		44.40%	
Keeling 2016	64	61							37.10%	50.30%		
Kim 2008												
Konety 2005	74	72			34.40%	51.40%			8.30%	18.40%		
Lucas 2006					34.30%	51.50%						
Maynard 2001	64	63			1%	1%			30.00%	34.00%		
Mehta 2016	66	62			25.30%	40.40%			39.10%	53.00%		
O'Neal 2014	64	61			25%	38%			37.20%	50.00%		
Pollock 2015	65	62		61	23.70%	44%		27.50%	37.10%	46.60%		61.20%
Rangrass 2014	74				30.50%				29.30%			
Rumsfeld 2002	63.6	62.2		63.8	1.10%	1.10%		0.50%	31.40%	38.10%		47.80%
Smith 2006	64.6	63.7			28.60%	45.70%			30.40%	47.20%		
Trivedi 2006												
Yeo 2007	66.91	63.17	65.6	64.02	25%	43%	27%	31%	33.00%	49.00%	47.00%	56%
Zacharias 2005	64	62			29.80%	46.10%			32.40%	43.40%		
Zindrou 2001	61.6		59.6		15.98%		19.70%		17.50%		43.00%	

Table 3. Study quality assessment using New Castle Ottawa Scale

Study	**Selection**	**Comparability**	**Exposure**	**Sum**
Anderson 2016	4	2	3	9
Andrews 2015	4	2	3	9
Becker 2006	4	0	3	7
Bridges 2000	4	0	3	7
Brister 2007	4	2	3	9
Chowdhury 2016	4	0	3	7
Cooper 2009	4	2	3	9
Efird 2015	4	0	3	7
Gasevic 2013	4	0	3	7
Goldsmith 1999	4	0	3	7
Gray 1996	4	2	3	9
Hadjinikolaou 2010	4	0	3	7
Kaila 2014	4	2	3	9
Keeling 2016	4	2	3	9
Kim 2008	4	2	3	9
Konety 2005	4	2	3	9
Lucas 2006	4	2	3	9
Maynard 2001	4	2	3	9
Mehta 2016	4	2	3	9
O'Neal 2014	4	0	3	7
Pollock 2015	4	0	3	7
Rangrass 2014	4	2	3	9
Rumsfeld 2002	4	2	3	9
Smith 2006	4	0	3	7
Trivedi 2006	4	2	3	9
Yeo 2007	4	0	3	7
Zacharias 2005	4	2	3	9
Zindrou 2001	4	0	3	7

Supplementary Table 1. Severity of coronary artery disease in studies included in the meta-analysis

Study	**EF (%)**						**Triple vessel disease (%)**					**Left main coronary artery disease (%)**				
	EF expressed as	**White**	**Black**	**Oriental**	**South Asian**	**Hispanic**	**White**	**Black**	**Oriental**	**South Asian**	**Hispanic**	**White**	**Black**	**Oriental**	**South Asian**	**Hispanic**
Anderson 2016																
Andrews 2015																
Becker 2006																
Bridges 2000	**Mean (SD)**	**51% (14)**	**48% (14)**				**70%**	**69%**				**20%**	**19%**			
Brister 2007							**76%**			**79%**		**22%**			**8%**	
Chowdhury 2016																
Cooper 2009	**Mean**	**50%**	**49%**									**23%**	**20%**			
Efird 2015							**66%**	**68%**				**21%**	**21%**			
Gasevic 2013							**28%**		**28%**	**27%**		**3%**		**5%**	**3%**	
Goldsmith 1999	**Good EF**	**52%**			**56%**		**63%**			**66%**						
Gray 1996							**64%**	**68%**				**24%**	**22%**			
Hadjinikolaou 2010	**EF ≥ 30%**	**93%**			**95%**											
Kaila 2014	**EF >35%**	**72%**			**68%**							**7%**			**6%**	
Keeling 2016	**Mean (SD)**	**52% (12)**	**50% (13)**													
Kim 2008																
Konety 2005																
Lucas 2006																
Maynard 2001																
Mehta 2016	**Median**	**55%**	**53%**				**95%**	**94%**				**32%**	**29%**			
O'Neal 2014							**67%**	**68%**				**26%**	**27%**			
Pollock 2015	**Mean (SD)**	**49% (14)**	**47% (16)**			**47% (14)**						**29%**	**28%**			**29%**
Rangrass 2014																
Rumsfeld 2002	**EF >35%**	**89%**	**87%**			**88%**	**72%**	**73%**			**76%**					
Smith 2006	**EF >40%**	**78%**	**75%**													
Trivedi 2006																
Yeo 2007	**EF >30%**	**92%**	**89%**			**89%**	**77%**	**77%**			**78%**	**24%**	**23%**			**23%**

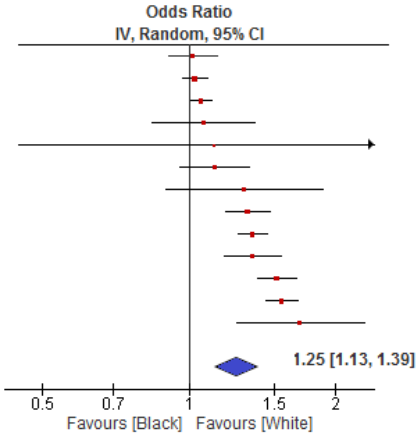
Zacharias 2005	Mean (SD)	50% (11)	49% (12)				72%	73%				19%	18%			
Zindrou 2001	EF >35%	88%			85%							1%			1%	

Supplementary Table 2. Methods and variables used in adjusting for hospital mortality

Study	Adjustment methods	Adjustment variables	
		Patient-level factors	**Hospital-level factors**
Andrews 2015	Logistic regression analysis	Age, age-gender interaction, gender	All patient refined DRG
Becker 2006	Logistic regression analysis	Admission type, gender, insurance status, procedure characteristics, SES, smoking, year of procedure, cardiomyopathy, COPD, CHF, CLD, CRF, CVD, dysrhythmias, DM, HD, HTN, MI, obesity, previous CABG, PVD, RF, unstable angina, valve disease	
Brister 2007	Logistic regression analysis	Age, EF, HTN & unstable angina	
Cooper 2009	Logistic regression analysis	Age, anticoagulants, Beta blockers, BMI, BSA, diuretics, EF, gender, height, IABP, immunosuppressive therapy, inotropes, nitrates, last creatinine level, resuscitation, smoking, status, weight, cardiogenic shock, COPD, CVA, CVD, DM, HD, HF, HLD, HTN, left main disease, MI, number of diseased vessels, PVD, RF	
Gasevic 2013	Logistic regression analysis	Age, distance from nearest hospital, gender, SES, time from MI to revascularization, arrhythmia, ARF, cancer, cardiogenic shock, CHF, CRF, CVD, DM, Severity of CAD	
Hadjinikolaou 2010	Logistic regression analysis	BMI, logistic Euroscore, DM, previous PCI	
Keeling 2016	Logistic regression analysis	Age, creatinine level, EF, gender, height, IABP, immunosuppressive therapy, resuscitation, single/multiple graft, status, weight, angina, arrhythmia, cardiogenic shock, COPD, CVD, DM, endocarditis, HF, HTN, MI, PAD, previous CV intervention, RF, valve disease	
Konety 2005	Logistic regression analysis	Admission priority, age, gender, SES, year of surgery, DM, CAD, CHF, COPD, CRF, CVD, HTN, PVD, previous CABG or PCI	
Lucas 2006	Logistic regression analysis	Age, gender, SES, urgency of admission, year of operation, Charlson comorbidity score	Hospital volume, clustering by hospital
Maynard 2001	Logistic regression analysis	Age, IMA grafting, Deyo score, COPD, DM, HTN, MI	
Mehta 2016	Logistic regression analysis	Patient characteristics, surgeon, SES	Hospital identity
Rangrass 2014	Logistic regression analysis	Age, emergency admission, gender, SES, Elixhauser comorbidity index	Hospital quality
Rumsfeld 2002	Linear regression analysis	Age, BSA, EF, gender, IMA graft use, number of anastomoses, preoperative ECG, preoperative diuretics & IV nitroglycerin, preoperative IABP, priority of surgery, serum creatinine, smoking, CAD, COPD, CVD,DM, HTN, MI, NYHA class, preoperative mortality risk, previous heart surgery, prior PCI, PVD, three vessel CAD	
Trivedi 2006	Logistic regression analysis	Age, gender, urgency of admission, COPD, CHF, DM, Elixhauser comorbidity index, PVD, HTN, MI	Hospital volume & clustering by hospital
Zacharias 2005	Logistic regression analysis	Age, Beta blockers, BSA, EF, gender, insurance status, preoperative IABP, priority of procedure, procedure characteristics, SES, smoking, arrhythmia, CHF, CVA, CVD, COPD, DM, double vessel disease, HLD, HTN, left main	

		disease, MI, NYHA class, obesity, PVD, RF, triple vessel disease, unstable angina.	

ARF: acute renal failure, BMI: body mass index, BSA: body surface area, CABG: coronary artery bypass graft, CAD: coronary artery disease, CHF: congestive heart failure, COPD: chronic obstructive pulmonary disease, CLD: chronic liver disease, CRF: chronic renal failure, CV: cardiovascular, CVA: cerebrovascular accident, CVD: cerebrovascular disease, DM: diabetes mellitus, DRG: diagnosis related group, HD: hemodialysis, HF: heart failure, HLD: hyperlipidemia, HTN: hypertension, IABP: intra-aortic balloon pump, IMA: internal mammary artery, IV: intravenous, MI: myocardial infarction, NYHA: New York Heart Association, PAD: peripheral arterial disease, PVD: peripheral vascular disease, RF: renal failure, SES: socioeconomic status



Central picture: Meta-analytic risk-adjusted estimates of race effect on operative mortality following CAGB (White as reference)

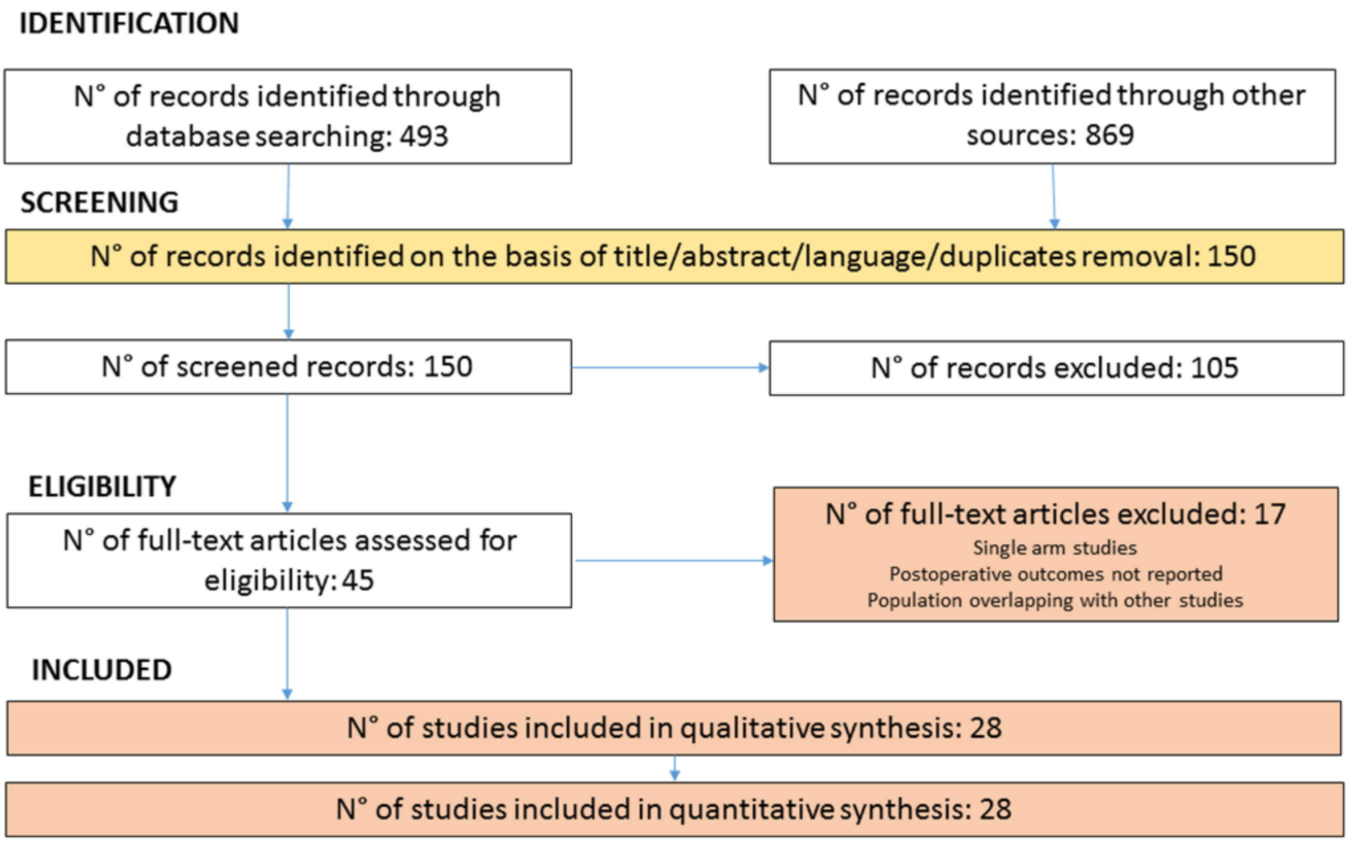
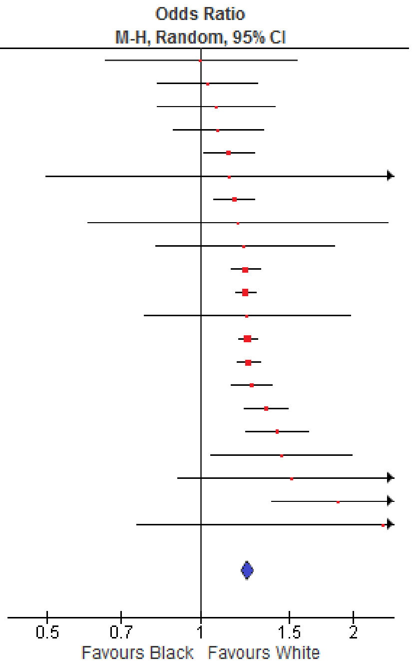


Figure 1. Study selection process for meta-analysis

A. Black vs white

Study or Subgroup	Black Events	Black Total	White Events	White Total	Weight	Odds Ratio M-H, Random, 95% CI
Yeo 2007	22	785	422	15069	0.5%	1.00 [0.65, 1.55]
Maynard 2001	86	2380	960	27439	1.7%	1.03 [0.83, 1.29]
Efird 2015	68	2379	303	11395	1.2%	1.08 [0.82, 1.41]
Rumsfeld 2002	107	2750	1056	29333	2.0%	1.08 [0.89, 1.33]
Mehta 2015	331	14375	2757	136362	5.4%	1.14 [1.02, 1.28]
Gray 1996	6	115	143	3113	0.1%	1.14 [0.49, 2.65]
Trivedi 2006	490	11393	7166	193684	7.4%	1.17 [1.07, 1.28]
Zacharias 2005	9	304	152	6073	0.2%	1.19 [0.60, 2.35]
Anderson 2016	26	975	315	14389	0.5%	1.22 [0.82, 1.84]
Bridges 2000	991	25850	17456	555939	11.8%	1.23 [1.15, 1.31]
Lucas 2006	2229	33367	45597	829037	16.9%	1.23 [1.18, 1.29]
Pollok 2015	20	612	169	6365	0.4%	1.24 [0.77, 1.98]
Becker 2006	2118	63991	27889	1040641	16.6%	1.24 [1.19, 1.30]
Konety 2005	1559	24354	29473	566785	14.6%	1.25 [1.18, 1.31]
Andrews 2015	538	15534	5367	194440	7.8%	1.26 [1.15, 1.38]
Rangrass 2014	438	9390	5567	159043	6.8%	1.35 [1.22, 1.49]
Kim 2008	233	8462	1241	63487	3.8%	1.42 [1.23, 1.64]
Keeling 2016	50	2810	168	13569	0.9%	1.45 [1.05, 1.99]
Smith 2006	22	644	44	1932	0.3%	1.52 [0.90, 2.55]
Cooper 2009	57	2033	195	12841	1.0%	1.87 [1.39, 2.52]
Chowdhury 2016	4	389	14	3107	0.1%	2.30 [0.75, 7.01]
Total (95% CI)		**222892**		**3884043**	**100.0%**	**1.24 [1.20, 1.28]**
Total events	9404		146454			

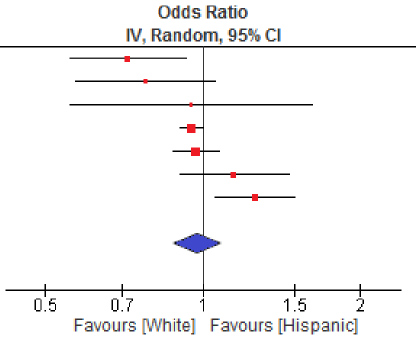
Heterogeneity: Tau² = 0.00; Chi² = 26.29, df = 20 (P = 0.16); I² = 24%
Test for overall effect: Z = 14.02 (P < 0.00001)



B. Hispanic vs white

Study or Subgroup	Hispanic Events	Hispanic Total	White Events	White Total	Weight	Odds Ratio IV, Random, 95% CI
Anderson 2016	73	4614	315	14389	11.0%	0.72 [0.56, 0.93]
Rumsfeld 2002	43	1525	1056	29333	8.6%	0.78 [0.57, 1.06]
Pollok 2015	15	593	169	6365	3.6%	0.95 [0.56, 1.62]
Becker 2006	1729	67554	27889	1040641	26.3%	0.95 [0.91, 1.00]
Trivedi 2006	410	11393	7166	193684	22.4%	0.97 [0.88, 1.08]
Yeo 2007	82	2561	422	15069	11.9%	1.15 [0.90, 1.46]
Rangrass 2014	132	3016	5567	159043	16.1%	1.26 [1.06, 1.51]
Total (95% CI)		**91256**		**1458524**	**100.0%**	**0.98 [0.87, 1.09]**
Total events	2484		42584			

Heterogeneity: Tau² = 0.01; Chi² = 18.08, df = 6 (P = 0.006); I² = 67%
Test for overall effect: Z = 0.45 (P = 0.66)



C. Asiatic vs white

Study or Subgroup	Asiatic Events	Asiatic Total	White Events	White Total	Weight	Odds Ratio IV, Random, 95% CI
Gasevic 2013	5	180	62	1507	5.2%	0.67 [0.26, 1.68]
Kaila 2014	4	252	17	737	4.0%	0.68 [0.23, 2.05]
Anderson 2016	66	3196	315	14389	17.6%	0.94 [0.72, 1.23]
Becker 2006	584	20353	27889	1040641	21.9%	1.07 [0.99, 1.17]
Yeo 2007	62	1772	422	15069	17.5%	1.26 [0.96, 1.65]
Zindrou 2001	24	436	41	1458	11.1%	2.01 [1.20, 3.37]
Brister 2007	29	1163	55	5028	12.5%	2.31 [1.47, 3.64]
Hadjinikolaou 2010	7	274	28	2623	6.0%	2.43 [1.05, 5.62]
Goldsmith 1999	13	194	5	190	4.2%	2.66 [0.93, 7.61]
Total (95% CI)		**27820**		**1081642**	**100.0%**	**1.33 [1.05, 1.69]**
Total events	794		28834			

Heterogeneity: Tau² = 0.07; Chi² = 25.95, df = 8 (P = 0.001); I² = 69%
Test for overall effect: Z = 2.33 (P = 0.02)

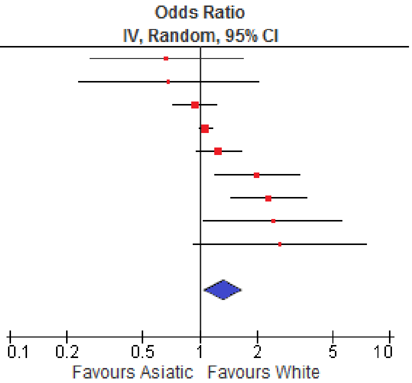
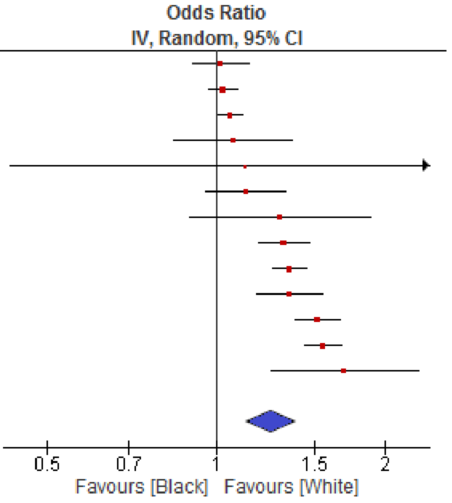


Figure 2. Meta-analytic unadjusted estimates of race effect on operative mortality following CABG (White as reference)

A. Black vs white

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Maynard 2001	0.0198	0.0582	8.9%	1.02 [0.91, 1.14]
Konety 2005	0.0296	0.0306	9.7%	1.03 [0.97, 1.09]
Lucas 2006	0.0583	0.0247	9.8%	1.06 [1.01, 1.11]
Rumsfeld 2002	0.0677	0.1235	6.5%	1.07 [0.84, 1.36]
Zacharias 2005	0.1212	0.4929	1.1%	1.13 [0.43, 2.97]
Trivedi 2006	0.1222	0.0832	8.0%	1.13 [0.96, 1.33]
Keeling 2016	0.2624	0.1876	4.5%	1.30 [0.90, 1.88]
Rangrass 2014	0.2776	0.0529	9.1%	1.32 [1.19, 1.46]
Becker 2006	0.3001	0.0352	9.6%	1.35 [1.26, 1.45]
Mehta 2015	0.3001	0.0687	8.6%	1.35 [1.18, 1.54]
Andrews 2015	0.4147	0.0464	9.3%	1.51 [1.38, 1.66]
Becker 2006	0.4383	0.0376	9.5%	1.55 [1.44, 1.67]
Cooper 2009	0.5247	0.1539	5.5%	1.69 [1.25, 2.28]
Total (95% CI)			**100.0%**	**1.25 [1.13, 1.39]**

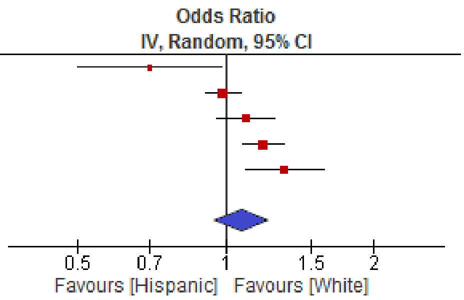
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 153.11$, df = 12 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: Z = 4.22 ($P < 0.0001$)



B. Hispanic vs white

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Rumsfeld 2002	-0.3567	0.1717	10.1%	0.70 [0.50, 0.98]
Becker 2006	-0.0101	0.043	25.3%	0.99 [0.91, 1.08]
Trivedi 2006	0.0953	0.0695	21.7%	1.10 [0.96, 1.26]
Becker 2006	0.174	0.0495	24.5%	1.19 [1.08, 1.31]
Rangrass 2014	0.2776	0.093	18.4%	1.32 [1.10, 1.58]
Total (95% CI)			**100.0%**	**1.08 [0.94, 1.23]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 19.03$, df = 4 ($P = 0.0008$); $I^2 = 79\%$
Test for overall effect: Z = 1.11 ($P = 0.26$)



C. Asiatic vs white

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Gasevic 2013	-0.4463	0.5935	5.4%	0.64 [0.20, 2.05]
Gasevic 2013	-0.0943	0.773	3.4%	0.91 [0.20, 4.14]
Becker 2006	0.0583	0.0613	38.4%	1.06 [0.94, 1.20]
Becker 2006	0.3507	0.0859	36.1%	1.42 [1.20, 1.68]
Hadjinikolaou 2010	0.72	0.52	6.7%	2.05 [0.74, 5.69]
Brister 2007	1.1314	0.4056	10.0%	3.10 [1.40, 6.86]
Total (95% CI)			**100.0%**	**1.33 [0.99, 1.77]**

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 15.68$, df = 5 ($P = 0.008$); $I^2 = 68\%$
Test for overall effect: Z = 1.92 ($P = 0.05$)

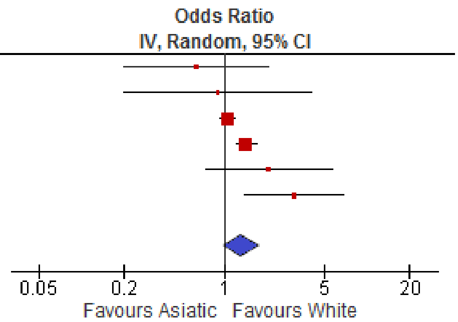


Figure 3. Meta-analytic risk-adjusted estimates of race effect on operative mortality following CABG (White as reference)

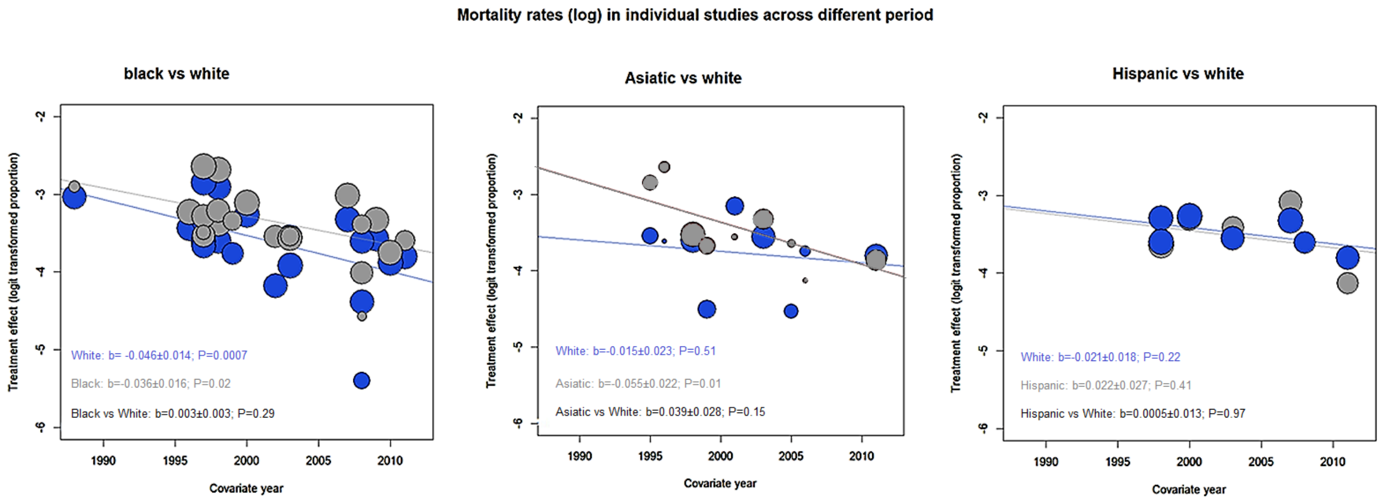
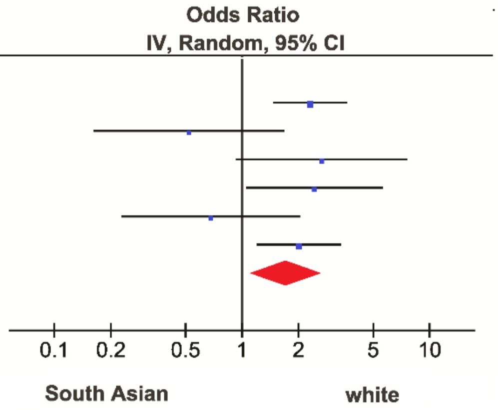


Figure 4. Meta-regression of crude mortality rate following CABG in the different ethnical groups and race effect on mortality across different study periods (median year of enrolment).

Unadjusted risk of mortality

Study or Subgroup	Asiatic Events	Asiatic Total	White Events	White Total	Weight	Odds Ratio IV, Random, 95% CI
South Asian vs white						
Brister 2007	29	1163	55	5028	8.8%	2.31 [1.47, 3.64]
Gasevic 2013	3	137	62	1507	3.0%	0.52 [0.16, 1.68]
Goldsmith 1999	13	194	5	190	3.5%	2.66 [0.93, 7.61]
Hadjinikolaou 2010	7	274	28	2623	4.8%	2.43 [1.05, 5.62]
Kaila 2014	4	252	17	737	3.3%	0.68 [0.23, 2.05]
Zindrou 2001	24	436	41	1458	8.0%	2.01 [1.20, 3.37]
Total (95% CI)		**2456**		**11543**	**31.3%**	**1.72 [1.12, 2.66]**
Total events	80		208			

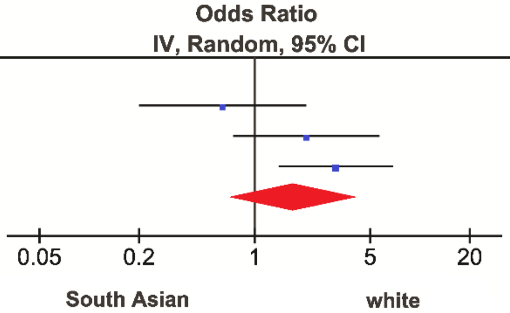
Heterogeneity: Tau² = 0.13; Chi² = 9.49, df = 5 (P = 0.09); I² = 47%
Test for overall effect: Z = 2.47 (P = 0.01)



Adjusted risk of mortality

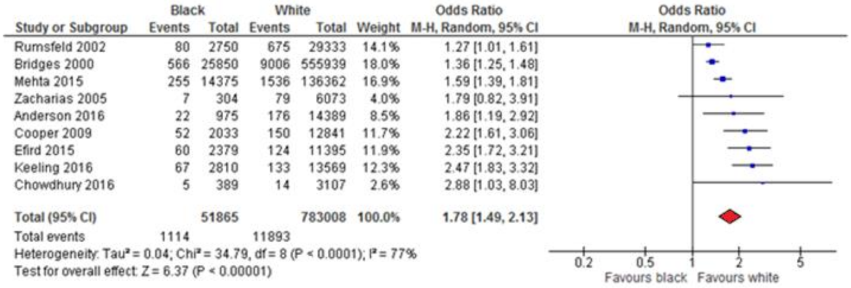
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
South Asian vs white				
Gasevic 2013	-0.4463	0.5935	5.0%	0.64 [0.20, 2.05]
Hadjinikolaou 2010	0.72	0.52	6.2%	2.05 [0.74, 5.69]
Brister 2007	1.1314	0.4056	9.0%	3.10 [1.40, 6.86]
Total (95% CI)			**20.3%**	**1.73 [0.71, 4.18]**

Heterogeneity: Tau² = 0.36; Chi² = 4.84, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 1.21 (P = 0.23)

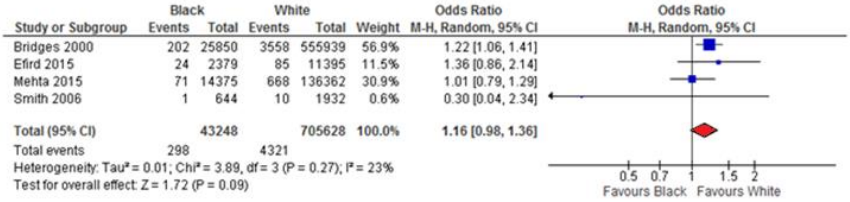


Supplementary Figure 1. Meta-analytic unadjusted and adjusted risk of operative mortality following CABG in South Asians compared to Whites.

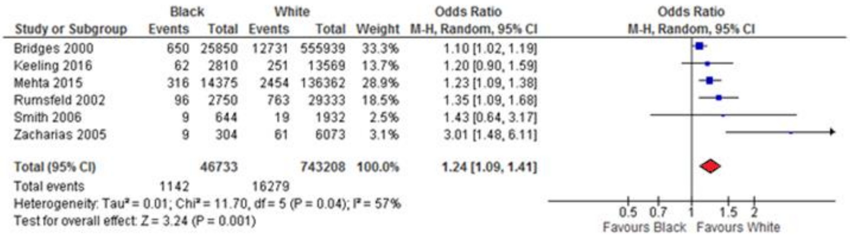
Stroke



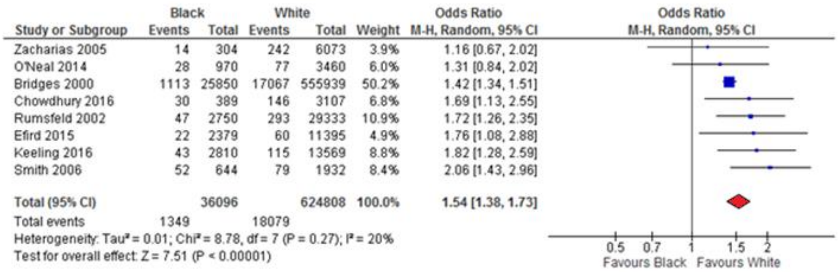
Wound infection



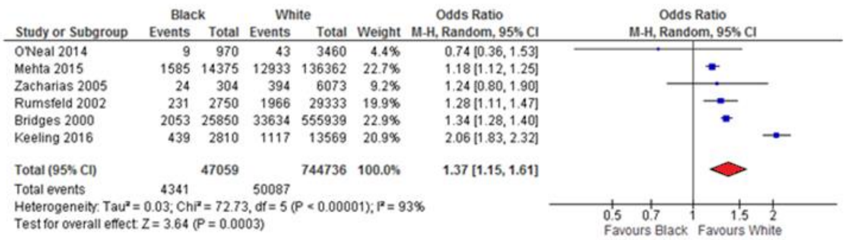
Bleeding



Renal Failure/Dialysis



Prolonged ventilation/Tracheostomy



Supplementary Figure 2. Meta-analytic point estimates of unadjusted effect of Black vs White race on postoperative complications following CABG.